

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

Claims 1-59. (Cancelled)

Claim 60. (Previously Presented): A method for inducing *ex vivo* proliferation of a population of T cells to sufficient numbers for use in therapy, comprising contacting a population of T cells *ex vivo* with a surface having covalently attached thereto:

(a) an anti-CD3 antibody or fragment thereof, which provides a primary activation signal to the T cells, thereby activating the T cells; and

(b) an anti-CD28 antibody or fragment thereof, which stimulates a CD28 accessory molecule on the surface of the T cells, thereby stimulating the activated T cells,

wherein the anti-CD3 antibody or fragment thereof and the anti-CD28 antibody or fragment thereof are covalently attached to the same surface,

the anti-CD3 antibody or fragment thereof and the anti-CD28 antibody or fragment thereof thereby inducing the population of T cells to proliferate to sufficient numbers for use in therapy.

Claim 61. (Previously Presented): The method of claim 60, wherein the anti-CD3 antibody is an anti-human CD3 monoclonal antibody.

Claim 62. (Previously Presented): The method of claim 60, wherein the anti-CD28 antibody is an anti-human CD28 monoclonal antibody.

Claim 63. (Previously Presented): The method of claim 60, wherein the anti-CD3 antibody or fragment thereof and the anti-CD28 antibody or fragment thereof, are covalently attached to the same surface using tosyl linkage.

Claim 64. (Previously Presented): The method of claim 60, further comprising:  
monitoring the proliferation of the T cells; and  
reactivating and re-stimulating the T cells with the the anti-CD3 antibody or fragment thereof and the anti-CD28 antibody or fragment thereof when the rate of T cell proliferation has decreased to induce further proliferation of the T cells.

Claim 65. (Previously Presented): The method of claim 64, wherein the step of monitoring proliferation of the T cells is by examining cell size or determining the level of expression of a cell surface molecule selected from the group consisting of B7-1, B7-2 and any combination thereof, and the step of reactivating and restimulating is initiated when T cell size has decreased or when the level of the cell surface molecule has decreased.

Claim 66. (Cancelled)

Claim 67. (Previously Presented): The method of claim 60, wherein the T cells are induced to proliferate to about 100-fold the original T cell population.

Claim 68. (Previously Presented): The method of claim 60, wherein the T cells are induced to proliferate to about 100,000-fold the original T cell population.

Claim 69. (Previously Presented): The method of claim 60, wherein the T cells are induced to proliferate for at least 3 days.

Claim 70. (Previously Presented): The method of claim 60, wherein the T cells are induced to proliferate for at least 7 days.

Claim 71. (Previously Presented): The method of claim 60, wherein the surface is a bead.

Claim 72. (Previously Presented): The method of claim 70, wherein the bead is a magnetic bead.

Claim 73. (Previously Presented): The method of claim 70, wherein the bead is a polystyrene bead.

Claim 74. (Previously Presented): The method of claim 60, wherein the surface is a cell surface.

Claim 75. (Previously Presented): The method of claim 60, wherein the surface is a tissue culture dish.

Claim 76. (Previously Presented): The method of claim 60, wherein the population of T cells are induced to proliferate to sufficient numbers for use in treating cancer.

Claim 77. (Previously Presented): The method of claim 60, wherein the population of T cells are induced to proliferate to sufficient numbers for use in treating an infectious disease.

Claim 78. (New): The anti-CD28 antibody of claim 62, wherein the antibody is 9.3 produced by the hybridoma assigned ATCC No. HB-10271.

Claim 79. (New): The anti-CD28 antibody of claim 62, wherein the antibody is EX 5.3D10 produced by the hybridoma assigned ATCC No. HB-11373.

**REMARKS**

Claims 60-65 and 67-77 are currently pending in this application.

Claims 78 and 79 have been newly added. Support for the newly added claims can be found at at page 8, lines 12-16 and lines 21-32.

Applicants provide herewith evidence of the availability of the 9.3 antibody. Ms. Marie Harris of the Patent Department at the American Type Culture Collection (ATCC) has indicated that the hybridoma that produces the 9.3 antibody, namely ATCC HB-10271, is available for distribution (*see*, Appendix A). In addition, Ms. Tanya Nunnally, a Patent Specialist at the ATCC has indicated that the hybridoma that produces the 9.3 antibody (ATCC HB-10271) is in stock and available for shipment immediately (*see*, Appendix B). As the Examiner is aware, the 9.3 antibody has been described in several journal articles and patents (*e.g.*, USPN 5,521,288). For the foregoing reasons, Applicants respectfully assert that the 9.3 antibody is a biological material that is accessible, because it is known and readily available to the public.

Regarding antibody EX5.3D10, Applicants note that the hybridoma that produces this antibody is deposited at ATCC Deposit No. HB-11373. Pursuant to the requirements of 37 C.F.R. § 1.806, Applicants note that the deposit shall be made for a term of at least thirty years and at least five years after the most recent request for the furnishing of a sample of the deposit was received by the depository. Furthermore, pursuant to the requirements of 37 C.F.R. § 1.808(a)((2), Applicants note that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the patent.

**CONCLUSION**

Upon entry of the instant amendment to the claims, claims 60-65 and 67-79 are pending in the instant application.

Applicants believe that all of the outstanding rejections of record have been overcome by amendment and/or argument. Accordingly, the claims are now believed to be in condition for allowance. Applicants respectfully request that the Examiner issue a timely Notice of Allowance.

No fees are believed to be due in connection with this correspondence. However, if any fees are due, please charge any payments due, or credit any overpayments, to our Deposit Account No. 08-0219.

The Examiner is invited to telephone the undersigned at the telephone number given below in order to expedite the prosecution of the instant application.

Respectfully submitted,

Dated: August 13, 2004

  
Colleen Superko  
Reg. No. 39,850

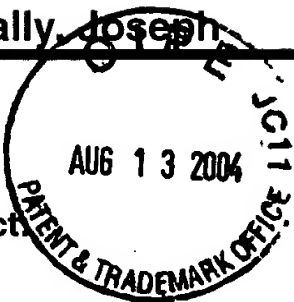
WILMER CUTLER PICKERING HALE AND DORR LLP  
60 State Street  
Boston, MA 02109  
Tel.: (617) 526-6564  
Fax: (617) 526-5000

**APPENDIX A**

Copy of correspondence dated August 9, 2004, between Ms. Marie Harris of the American Type Culture Collection (ATCC) Patent Department and Joseph J. Koipally, Ph.D. of Wilmer Cutler Pickering Hale and Dorr LLP regarding the availability of ATCC deposit HB-10271.

Koipally, Joseph

From: Harris, Marie [Mharris@atcc.org]  
Sent: Monday, August 09, 2004 10:11 AM  
To: Koipally, Joseph  
Subject: RE: HB-10271



Hi Dr. Koipally,  
The price for HB-10271 is \$200 (plus shipping and handling). I believe that Customer Service at this point would request that you complete the Sales Order Form (which can be obtained from our website) and place the order online or by fax or phone. Is there any other information that you need before you place the order?

Sincerely,  
Marie

-----Original Message-----

From: Koipally, Joseph [mailto:Joseph.Koipally@wilmerhale.com]  
Sent: Monday, August 09, 2004 9:58 AM  
To: Harris, Marie  
Subject: RE: HB-10271

Dear Ms. Harris,

Thank you for your response.

I have contacted Customer Service to obtain quote and availability information for ATCC HB-10271 and I faxed a request on August 5, 2004 to (703)365-2750 but have yet to receive the requested information. I had asked that the quote and availability information be faxed to me at (617) 526-5000.

Your assistance in obtaining the requested information would be greatly appreciated.

Thank you for your time.

Sincerely,  
Joseph Koipally

-----Original Message-----

From: Harris, Marie [mailto:Mharris@atcc.org]  
Sent: Monday, August 09, 2004 9:54 AM  
To: Koipally, Joseph  
Subject: HB-10271

Dear Dr. Koipally,

Thank you for your inquiry. ATCC HB-10271 is available for distribution. It is not however listed on our website. The item was deposited for patent purposes and when we became aware of the issuance of a U.S. Patent we made it available for distribution. Only those items that have been authenticated by the ATCC are actually listed on our website catalog. You may contact our Customer Service Department and place an order (you may use our online shopping cart to place your order electronically or download the fax order form and fax it to 703-365-2750 or call 800-638-6597). There is no technical information on patent strains. You may want to look at the U.S. Patent which issued for this item (5,521,288 dated May 28, 1996).

Sincerely,  
Marie Harris

ATCC Patent Department  
mharris@atcc.org

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**APPENDIX B**

Copy of facsimile letter dated August 11, 2004 from Ms. Tanya Nunnally, Patent Specialist at the ATCC to Joseph J. Koipally, Ph.D., at Wilmer Cutler Pickering Hale and Dorr LLP indicating the commercial availability of the hybridoma producing the 9.3 antibody (ATCC Deposit No. HB-10271).

**AMERICAN TYPE CULTURE COLLECTION**

10801 University Boulevard  
Manassas, VA 20110-2209 USA  
Telephone: 703-365-2700

**FACSIMILE**

**Date:** August 11, 2004

**To:** Joseph J. Koipally, Ph.D.  
Wilmer Cutler Pickering Hale and Dorr LLP

**Fax Number:** 617-526-5000


**Total number of pages including this page:** 2

**From:** ATCC Patent Depository

**ATCC Patent Depository Fax Number:** 703-365-2745

**Reference:** Patent Deposit, ATCC No. HB-10271

Attached is the information you requested concerning the availability of the patent deposit, Hybridoma, 9.3 Assigned ATCC No. HB-10271. I am unable to provide you with a formal quote as an established ATCC account number is required for quotations. However, this document indicates the item is in stock and available for shipment immediately. If you need further assistance please contact me. Thank you.



Tanya Nunnally, Patent Specialist  
ATCC Patent Depository  
Tel.: 703-365-2721  
nunnally@atcc.org

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# ATCC



organization dedicated to biological standards and biodiversity

10801 University Boulevard  
Manassas, Virginia 20110-2209 USA

Telephone: (703) 365-2700  
Facsimile: (703) 365-2701  
Internet: <http://www.atcc.org/>

## Customer Quick Quote

08/11/04

Sold-To:  
Item Number: HB-10271

Effective Date: 08/11/04  
Currency: USD

```
List Price: 200.00
Net Price: 200.00
Customer: Profit Company
Country: USA
Item Number: HB-10271
Part Desc: Murine Hybridoma 9.3
```

Discount: 0.0  
Extended Price: 200.00

Ctlg Comments:

Form: FZ  
BSL: 1

Ship Date (if ordered today): 08/12/04

Mfg LT: 0  
Qty Avail: 9.0